UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/029,016	12/20/2001	Anthony J. Celeste	5205BD1	4438

7590 09/02/2004

FINNEGAN HENDERSON FARABOW GARRETT AND DUNNER LLP
1300 I STREET NW
WASHINGTON, DC 20005-3315

EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/029,016	CELESTE ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *7-24* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1201,0604*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 06/21/2004 has been entered. Claims 7-24 are pending.

Applicant's election with traverse of Group II, claims 7-24, inasmuch as they pertain to a method comprising the administration of a BMP-11 polypeptide comprising the amino acid sequence of SEQ ID NO: 11, in the reply filed on 06/21/2004 is acknowledged. The traversal is on the ground(s) that this restriction requirement is improper because the Examiner has not shown that it would be a burden to examine the claims together, the law requires that both (1) the inventions are independent and distinct, and (2) there would be a serious burden on the Examiner if restriction was not required, the Examiner has focused on only the first part of this two-part test, the Examiner needs to show that there would be a serious burden in examining the claims together, Applicants believe that there would not be a serious burden in examining the groups together, the groups are directed to methods for-using bovine and human BMP-11 sequences in the same class and subclasses, Applicants believe searches could easily be constructed to identify any prior art to both sequences. This is not found persuasive because sequences encompassing different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such sequence is presumed to represent an independent and distinct invention and each such sequence requires a separate search, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7, 10, 13, 16, 19, 22 link(s) inventions I and II. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 7, 10, 13, 16, 19, 22. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler,* 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 10, 13, 16, 19, 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention. The claims are indefinite over the recitation of "BMP-11."

The following passages from the specification seem most relevant for construing the term "BMP-11" and the claims:

> Further included in the present invention are DNA sequences which hybridize under stringent conditions with the DNA sequence of SEQ ID NO: 1 or SEQ ID NO: 10 and encode a protein having BMP-11 activity. Finally, allelic or other variations of the sequences of SEQ ID NO: 1 or SEQ ID NO: 10, whether such nucleotide changes result in changes in the peptide sequence or not, but where the peptide sequence still has BMP-11 activity, are also included in the present invention. Page 9, lines 4-11.
>
> The BMP-11 proteins provided herein also include factors encoded by the sequences similar to those of SEQ ID NO: 1 or SEQ ID NO: 10, but into which modifications are naturally provided (e.g. allelic variations in the nucleotide sequence which may result in amino acid changes in the polypeptide) or deliberately engineered. For example, synthetic polypeptides may wholly or partially duplicate continuous sequences of the amino acid residues of SEQ ID NO: 2 or SEQ ID NO: 11. These sequences, by virtue of sharing primary, secondary, or tertiary structural and conformational characteristics with inhibin-.beta. polypeptides of SEQ ID NO: 2 or SEQ ID NO: 11 may possess BMP-11 activity in common therewith. Thus, they may be employed as biologically active substitutes for naturally-occurring BMP-11 polypeptides in therapeutic processes. Paragraph bridging pages 12-13.
>
> Similarly, DNA sequences which code for BMP-11 proteins coded for by the sequences of SEQ ID NO: 1 or SEQ ID NO: 10, but which differ in codon sequence due to the degeneracies of the genetic code or allelic variations (naturally-occurring base changes in the species population which may or may not result in an amino acid change) also encode the novel factors described herein. Variations in the DNA sequences of SEQ ID NO: 1 or SEQ ID NO: 10 which are caused by point mutations or by induced modifications (including insertion, deletion, and substitution) to enhance the activity, half-life or production of the polypeptides encoded are also encompassed in the invention. Page 14, full paragraph 1.

The instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "BMP-11." Therefore, an

artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claims 7-15, 22-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 7-15, 22-24 are indefinite because they lack a process step which clearly relates back to the claim preamble and it is unclear what process is to be achieved; an intended use is not the same as achieving a result; in the absence of a recitation as to any result, or a process step producing a result, it is unclear what result of the process can be inferred. The metes and bounds are not clearly set forth.

Claims 22-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 22-24 are indefinite because it is unclear to whom or what the compound is being administered. The metes and bounds are not clearly set forth.

Claims 7-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of promoting neuronal cell survival, does not reasonably provide enablement for a method of modulating or inducing neuronal cell/tissue development, formation, growth differentiation, proliferation or maintenance. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Prior to 11/07/1997 (the filing date of U. S. Application No. 08/966,297) the disclosure only contemplates that BMP-11 may be useful in promoting neuronal cell survival, referring to Schubert et al., Nature, 344:868-870 (1990). In U. S. Application No. 08/966,297 (filed 11/07/1997) it is disclosed that BMP-11 promotes survival of PC12 cells under serum-free conditions, that BMP-11 induces neurite formation in PC12 cells and BMP-11 therefore induces neuronal differentiation, and that BMP-11 induces neuronal cell formation and protects, maintains, heals, and repairs neuronal tissue in peripheral neuropathy disorders.

The term "modulating neuronal cell development" encompasses achieving any and/or all desired effects. The specification has not shown how to achieve, for example, inhibition of neurite formation with an inducer of neurite formation, or how to achieve, for example, inhibition of neuronal cell growth with an inducer of neuronal cell growth.

The term "inducing neuronal cell formation" encompasses the formation of neuronal cells from non-neuronal tissues, such as liver, kidney, lung, spleen, or intestine. There is simply no nexus between the teaching of the present specification or of the prior art of record and the formation of neuronal cells or tissues from any and/or all cells or tissues, including non-neuronal cells or tissues.

The claims are also directed to or encompass modulating or inducing any and/or all neuronal cell/tissue development, formation, growth differentiation, proliferation or maintenance.

Schubert (CB, cited by Applicants) teaches that activin did not increase the survival of ciliary ganglion cells or of several glial cell lines (page 869, right column, last full paragraph). Schubert does not indicate that any and/or all BMPs would successfully modulate or induce any and/or all neuronal cell/tissue development, formation, growth differentiation, proliferation or maintenance.

Jordan teaches:

> BMPs 9 and 11 did not promote the in vitro survival of dopaminergic neurons (page 1703, paragraph bridging left and right columns).
>
> BMP-11 had no effect on BrdU incorporation and astroglial cell maturation, indicating that not all members of the BMP family share effects on proliferation and differentiation of cells in the astrocyte lineage (page 1703, right column, full paragraph 1).
>
> BMPs are distinct from each other with regard to their neurotrophic potentials (page 1705, left column, full paragraph 1). The BMPs are heterogeneous with regard to the their biological effects (paragraph bridging pages 1705-1706).

Jordan is evidence that the skilled artisan would not expect that any and/or all BMPs, nor BMP-11 in particular, would successfully modulate or induce any and/or all neuronal cell/tissue development, formation, growth differentiation, proliferation or maintenance. Jordan is also evidence that the effects of BMPs are unpredictable.

The specification lacks guidance for, and working examples of, modulating or inducing any and/or all neuronal cell/tissue development, formation, growth differentiation, proliferation or maintenance. The examiner is aware that working examples are not required. However, the lack of working examples is a factor to be considered. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art, and the

limited content of the present disclosure, the skilled artisan is left to perform an undue amount of unduly extensive experimentation in order to practice the full scope of the claimed invention. It would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6340668, and, if necessary, in view of Wozney (A). U.S. Patent No. 6340668 claims in vitro and in vivo methods of promoting the survival of neuronal cells with a BMP-11 protein comprising the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 11. The BMP-11 protein comprising the amino acid sequence of SEQ ID NO: 11, as recited in the patented claims, comprises an amino acid sequence from amino acid 1 to amino acid 109 or from amino acid 7 to 108 of SEQ ID NO: 11, as recited in the pending claims. In performing the methods of the patented claims one of ordinary skill in the art would necessarily

prepare a composition comprising a purified BMP-11. The examiner includes Wozney (A) in the statement of the rejection only if it is necessary to show that it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to prepare and use a purified BMP-11 comprising an amino acid sequence from amino acid 1 to amino acid 109 of SEQ ID NO: 11, as taught by Wozney (A) (claim 1), with a reasonable expectation of success. One of ordinary skill in the art would be motivated to prepare and use a BMP-11 comprising an amino acid sequence from amino acid 1 to amino acid 109 of SEQ ID NO: 11 because it is the mature active portion of the molecule. Although the claims of U.S. Patent No. 6340668 do not teach recovering the neuronal cells, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to recover the neuronal cells with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to perform further biochemical or biologic analysis of the neuronal cells. Neuronal cells are neuronal tissue in the absence of evidence to the contrary. The intended uses of the presently claimed methods do not patentably distinguish the present claims from the patented claims.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Mason (V) constructed a series of activin mutants were constructed in which the nine cysteine residues (amino acids 4, 11, 12, 40, 44, 80, 81, 113, and 115) in the mature 116-amino acid beta-subunit were individually altered to alanine residues. Alanine substitution at either cysteine residues 4 or 12 did not interfere

with homodimer formation, but the mutant activin A molecules had reduced biological and receptor binding activity (2- to 3-fold). See the Abstract.

Lee (U. S. Patent No. 5914234) discloses that GDF-11 may have neurotrophic activities for other neuronal populations. Hence, GDF-11 may have in vitro and in vivo applications in the treatment of neurodegenerative diseases, such as amyotrophic lateral sclerosis, or in maintaining cells or tissues in culture prior to transplantation. See paragraph bridging columns 3-4.

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571)272-0961.

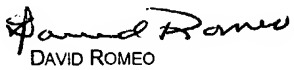
IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
2004-08-28